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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,759	12/08/2003	David John King	CARP0007-101	4275

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EXAMINER	
TUNGATURTHI, PARITHOSH K	
ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/731,759	KING ET AL.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/13/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The applicant has timely traversed the non-final rejection in the reply filed on 03/06/2007, and a response to the arguments is set forth.

2. Claims 1-10 have been cancelled

3. Claims 11-16 have been newly added and are under examination.

Rejections Withdrawn

4. The rejection of claims 3-7 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of amendments to the claims.

5. The rejection of claims 1-7, 9 and 10 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antigen binding antibody fragments, Fab and Fab', does not reasonably provide enablement for just any antibody fragments is withdrawn in view of amendments to the claims.

6. The rejection of claims 1-4 and 6-10 under 35 U.S.C. 102(b) as being anticipated by Pedley et al (Br. J. Cancer. 1994. 70:1126-1130; IDS – 12/13/2004) is withdrawn in view of amendments to the claims.

7. The rejection of claims 1, 9 and 10 under 35 U.S.C. 102(e) as being anticipated Griffiths et al (U.S. Patent 5,670,132, Date Filed: 09/20/1994; IDS – 12/13/2004) is withdrawn in view of amendments to the claims.

8. The rejection of claims 1-10 under 35 U.S.C. 103(a) as being unpatentable over Pedley et al (Br. J. Cancer. 1994. 70:1126-1130; IDS – 12/13/2004) in view of Goodson et al (BioTechnology. 1990. 8:343-346; IDS – 12/13/2004) and in view of Woghiren et al (Bioconjugate Chem. 1993. 4:314-318; IDS – 12/13/2004) is withdrawn in view of amendments to the claims.

New Grounds of Rejections

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 11-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Zapata[a] et al (FASEB J. 1995. 9:A1479; IDS – 12/13/2004).

The claims are drawn to a modified monovalent antibody fragment which is a Fab' wherein the CH1 is extended to provide a hinge domain which contains only one cysteine residues which is covalently linked through it sulphur atom to a polymer

molecule, wherein the polymer is a substituted, straight or branched chain polyalkelene, poly(ethylene glycol), methoxy(polytheylene glycol).

Zapata[a] et al teach a Fab' fragment which contains a single cysteine in the hinge region including the coupling of monomethoxypoly(ethylene glycol) to the cysteine.

Thus, Zapata[a] et al anticipate the instant claims.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zapata[a] et al (FASEB J. 1995. 9:A1479) and further in view of Zapata[b] et al (U.S. Patent 6214984, Continuation Date 04/20/1995; IDS – 12/13/2004).

Claims 11-16 have been described supra. Claims 15 and 16 are drawn to an antibody fragment of claim 11 covalently attached to one or more effector or reporter molecules and a pharmaceutical composition comprising such antibody fragment with one or more pharmaceutically acceptable excipients, diluents or carriers.

Zapata[a] et al has been described supra.

Zapata[a] et al does not teach a composition with a carrier or fragment with an effector or reporter molecule. These deficiencies are made up for in the teachings of Zapata[b] et al.

Zapata[b] et al teach a Fab' fragment that has been engineered to have one cysteine in the hinge (see column 17, lines 35-43) and the antibody fragment can be labeled with a reporter molecule (see column 14, lines 29-37) and compositions comprising carriers (see column 15, lines 9-36).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antigen binding fragment with PEG as taught by Zapata[a] et al and label the fragment and produce compositions comprising a carrier and the antibody as taught by Zapata[b] et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antigen binding fragment with PEG as taught by Zapata[a] et al and label the fragment and produce compositions comprising a carrier and the antibody as taught by Zapata[b] et al because Zapata[a] et al teach "the ability to modify the clearance rate of an antibody Fab' fragment by attaching a single MePEG moiety at a unique site, without affecting antigen binding, increases significantly the potential therapeutic value of this type of molecule". In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antigen binding fragment with PEG as taught by Zapata[a] et al and label

the fragment and produce compositions comprising a carrier and the antibody as taught by Zapata[b] et al because Zapata[b] et al teach therapeutic applications for CD18 with anti-CD18 antibody fragments and these fragments can be labeled with a detectable moiety and the antibodies can be used in therapeutic applications when combined with acceptable carriers (see column 14 and column 15). In addition, it would have been obvious to one of skill in the art to label antibody fragments for detection or therapy and to formulate compositions comprising a carrier for therapeutic applications.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

13. Claims 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobs et al (U. S. Patent 5,853,723, filed 9/20/96; IDS – 12/13/2004) and further in view of Bodmer et al (WO 89/01974, published 3/9/89; IDS – 12/13/2004).

The claims have been described supra.

Jacobs et al teach methoxy-PEG coupled to a Fab' fragment through a hinge cysteine residue and compositions comprising excipients and the fragments can be labeled (see column 7, lines 25-41, 62-67, column 8, lines 35-40, and Figure 1 and 2). Jacobs et al does not specifically teach the Fab' with a single cysteine residue in the hinge. This deficiency is made up for in the teachings of Bodmer et al.

Bodmer et al teach reducing the cysteines in the hinge to one for the purpose of attaching other molecules (see page 7) and to reduce the complexity of subsequent chemical additions at the hinge (see page 10, Example 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have reduced the number of cysteine residues in the hinge to one as taught by Bodmer et al and produce a Fab'-PEG antigen binding fragment as taught by Jacobs et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have reduced the number of cysteine residues in the hinge to one as taught by Bodmer et al and produce a Fab'-PEG antigen binding fragment as taught by Jacobs et al because Jacobs et al teach the polymer provides a hydration shell around the monoclonal antibody or fragment for inhibiting immune recognition (see column 6, lines 5-10). In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have reduced the number of cysteine residues in the hinge to one as taught by Bodmer et al and produce a Fab'-PEG antigen binding fragment as taught by Jacobs et al because Bodmer et al teach by reducing the cysteine residues in the hinge to one this reduces the complexity of subsequent chemical additions to the hinge. In addition, it would have been obvious to one of skill in the art to label antibody fragments for detection or

therapy and to formulate compositions comprising a carrier for therapeutic applications as which are taught by Jacobs et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

14. No claims are allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

17. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi Ph.D.
(571) 272-8789

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER